FILE 'CAPLUS' ENTERED AT 16:05:52 ON 04 SEP 2003

FILE 'MEDLINE' ENTERED AT 16:05:52 ON 04 SEP 2003

=> S VACCINE
L1 158383 VACCINE

=> S BETA AMYLOID
L2 9476 BETA AMYLOID

=> S ADJUVANT AND L2
L3 32 ADJUVANT AND L2

=> S L3 AND L1
L4 18 L3 AND L1

=> D 1-18 CBIB ABS

L4 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
2003:154273 Document No. 138:203657 Amyloid precursor protein or . ***beta*** . ***amyloid*** conjugated with B or T cell epitope as ***vaccine*** against Alzheimer's disease. Rasmussen, Peter Birk; Jensen, Martin Roland; Nielsen, Klaus Gregorius; Koefoed, Peter; Dal Degan, Florence (Pharmexa A/S, Den.). PCT Int. Appl. WO 2003015812 A2 20030227, 122 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-DK547 20020820. PRIORITY: DK 2001-1231 20010820; US 2001-PV337543 20011022; DK 2002-558 20020416; US 2002-PV373027 20020416.

AB Disclosed are novel methods for combating diseases characterized by deposition of amyloid. The methods generally rely on immunization against amyloid precursor protein (APP) or . ***beta*** . ***amyloid*** (A.beta.). Immunization is preferably effected by administration of analogs of autologous APP or A.beta., said analogs being capable of inducing antibody prodn. against the autologous amyloidogenic polypeptides. Esp. preferred as an immunogen is autologous A.beta. which has been modified by introduction of one single or a few foreign, immunodominant and promiscuous T cell, B cell or T helper cell epitopes. Also disclosed are nucleic acid vaccination against APP or A.beta. and vaccination using live ***vaccines*** as well as methods and means useful for the vaccination against Alzheimer's disease. Such methods and means include methods for the prepn. of analogs and pharmaceutical formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and pharmaceutical formulations.

L4 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
2002:927177 Document No. 138:23639 Amyloid .beta. peptide fragment linked to helper T cell epitope for prevention and treatment of Alzheimer's disease. Wang, Chang Yi (United Biomedical, Inc., USA). PCT Int. Appl. WO 2002096350 A2 20021205, 77 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US10293 20020402. PRIORITY: US 2001-865294 20010525.

AB The present invention relates to a compn. comprising a peptide immunogen useful for the prevention and treatment of Alzheimer's Disease. More particularly, the peptide immunogen comprises a main functional/regulatory site, an N-terminal fragment of Amyloid .beta. (A.beta.) peptide linked to a helper T cell epitope (Th) having multiple class II MHC binding motifs. The peptide immunogen elicit a site-directed immune response against the

main functional/regulatory site of the A.beta. peptide and generate antibodies, which are highly cross-reactive to the sol. A.beta.1-42 peptide and the amyloid plaques formed in the brain of Alzheimer's Disease patients. The antibodies elicited being cross reactive to the sol. A.beta.1-42 peptide, promote fibril disaggregation and inhibit fibrillar aggregation leading to immunoneutralization of the "sol. Asz-derived toxins"; and being cross-reactive to the amyloid plaques, accelerate the clearance of these plaques from the brain. Thus, the compn. of the invention comprising the peptide immunogen is useful for the prevention and treatment of Alzheimer's Disease.

L4 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

2002:708232 Document No. 137:215367 . ***beta*** .- ***Amyloid*** immunization approaches for Alzheimer's disease. Imbimbo, Bruno P. (Research & Development Department, Chiesi Farmaceutici, Parma, 43100, Italy). Drug Development Research, 56(2), 150-162 (English) 2002. CODEN: DDREDK. ISSN: 0272-4391. Publisher: Wiley-Liss, Inc..

AB A review. Alzheimer's disease (AD) represents the third leading cause of death in the U.S. and the leading cause of dementia in the elderly population. Until recently, there was little hope of efficiently combating this devastating disease. The deposition of . ***beta*** .- ***amyloid*** (A.beta.) is the major pathol. hallmark of AD brains. Genetic, biochem., and pharmacol. evidence support the hypothesis that A.beta. plays a key role in the development of the disease. Thus, in the last 5 yr a no. of pharmacol. strategies have been developed to interfere with the A.beta. cascade. The most revolutionary of these approaches was proposed in 1999 by scientists at Elan Pharmaceuticals, which immunized against A.beta. transgenic mice with spontaneously developing A.beta. pathol. The immunization was achieved by s.c. injections of a preaggregated form of the synthetic human 42-amino acid A.beta. emulsified with Freund's ***adjuvant*** , an immune stimulant. The vaccination caused a near complete inhibition of A.beta. plaque formation in younger animals and a marked redn. of the A.beta. burden in older animals. The effects on A.beta. plaques were accompanied by a redn. of A.beta.-assocd. astrogliosis and neuritic dystrophy. These results were later confirmed by other groups with similar vaccination protocols, which also demonstrated that the A.beta. immunization of transgenic animals normalize or reduce the cognitive impairment assocd. with A.beta. pathol. Interestingly, effective removal of brain A.beta. plaques was also obtained by peripherally administering A.beta. antibodies. The mechanism with which the ***vaccine*** increases A.beta. clearance is not fully understood. Centrally, the ***vaccine*** appears to activate A.beta. phagocytosis by microglial monocytes. Peripherally, serum A.beta. antibodies bind and sequester A.beta., thus altering its equil. between CNS and plasma. The dramatic results obtained in animal models of AD raised unprecedented hopes for both a preventive and a curative intervention for this devastating disorder. A ***vaccine*** prepn. for human use (AN-1792) composed of preaggregated human A.beta.42 peptide and a highly purified saponin deriv. (QS-21) was developed by Elan Pharmaceuticals and Wyeth Ayerst and tested in AD patients. Unfortunately, a Phase IIa study aimed at evaluating the safety and immunol. activity of AN-1792 in 360 AD patients was discontinued because 15 subjects receiving the ***vaccine*** developed serious signs of CNS inflammation. Both central activation of cytotoxic T cells and autoimmune reactions were proposed as potential mechanisms of toxicity. Other therapeutic A.beta. vaccination strategies are being pursued, including immuno-conjugates and monoclonal antibodies. The future of these and other A.beta. immunization approaches depend on a clear understanding of the mechanism of A.beta. clearance and addnl. insight into the role of inflammation in the AD brain.

L4 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

2002:658588 Document No. 137:184455 Synthetic ***vaccine*** agents. Nielsen, Klaus Gregorius; Koefoed, Peter (Den.). U.S. Pat. Appl. Publ. US 2002119162 A1 20020829, 16 pp., Cont.-in-part of U.S. Ser. No. 785,215. (English). CODEN: USXXCO. APPLICATION: US 2002-80101 20020219. PRIORITY: WO 2001-DK113 20010219; US 2001-785215 20010220; DK 2001-1231 20010820; US 2001-PV337543 20011022.

AB The present invention provides for novel immunogens that are comprised of an activated polyhydroxypolymer backbone to which is attached 2 sep. antigenic determinants. The 1st antigenic determinant includes a B-cell

or CTL epitope and the 2nd antigenic determinant includes a T-helper epitope. In preferred embodiments, the antigenic determinants are derived from different mols. and species. Exemplary immunogens of the invention are constituted of a linear tresyl-activated dextran backbone to which is coupled B-cell or CTL epitopes of an antigen and to which is also coupled universal T-helper epitopes. Also disclosed are immunogenic compns. comprising the immunogens, methods of immunization and a method for identification of suitable immunogens of the invention. The examples discuss the synthesis of a . ***beta*** .- ***amyloid*** peptide copolymer ***vaccine*** , antibody titer detn., and assays to monitor CTL activity.

L4 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
2002:368339 Document No. 136:384964 ***Vaccine*** formulations comprise antigen, allergen, autoantigen or tumor antigen and immune ***adjuvant*** containing aminoalkyl glucosamine phosphate compound in combination with cytokine or lymphokine. Hagen, Michael (American Cyanamid Company, USA). PCT Int. Appl. WO 2002038177 A2 20020516, 94 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US46943 20011108. PRIORITY: US 2000-PV247100 20001110; US 2001-PV330345 20011018.
AB The use of an aminoalkyl glucosamine phosphate compd., or a deriv. or analog thereof, in combination with a cytokine or lymphokine such as granulocyte macrophage colony stimulating factor or interleukin-12, is useful as an ***adjuvant*** combination in an antigenic compn. to enhance the immune response in a vertebrate host to a selected antigen. The aminoalkyl glucosamine phosphate compd. is RC 529; and the antigen is an antigen derived from pathogenic virus, bacterium, fungus or parasite, autoantigen such as amyloid precursor protein or . ***beta*** .- ***amyloid*** peptide, tumor-assocd. antigen, or allergen.

L4 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
2002:332217 Document No. 136:339487 Fusion proteins comprising . ***beta*** .- ***amyloid*** peptide and heat shock protein for immunization treatments of Alzheimer's disease. Ghirardi, Silvia; Armani, Elisabetta; Amari, Gabriele; Puccini, Paola; Imbimbo, Bruno; Villetti, Gino (Chiesi Farmaceutici S.P.A., Italy; Ghirardi Silvia). PCT Int. Appl. WO 2002034777 A1 20020502, 33 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-EP12242 20011023. PRIORITY: IT 2000-MI2299 20001024.
AB The present invention is related to fusion proteins (A.beta.-Hsp) (III) and their use in the treatment or prophylaxis of disorders assocd. with an accumulation of . ***beta*** .- ***amyloid*** , specifically in patients with Alzheimer's disease. Said fusion proteins are derived from the condensation of . ***beta*** .- ***amyloid*** protein or fragments thereof (A.beta.) with a heat shock protein (Hsp). The . ***beta*** .- ***amyloid*** peptide is human . ***beta*** .- ***amyloid*** peptide (1-39), (1-40) or (1-42); and the heat shock protein is Hsp25, Hsp27, Hsp28, Hsp60, Hsp70 or Hsp90.

L4 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
2002:185445 Document No. 136:246397 Chimeric antibody comprising fragment of anti-. ***beta*** .- ***amyloid*** monoclonal antibody 6C6 and transferrin fragment for treating and diagnosing amyloidosis-associated diseases. Nicolau, Yves Claude (Aventis Pharma S.A., Fr.; Universite Louis Pasteur). PCT Int. Appl. WO 2002021141 A2 20020314, 54 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ,

CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US27632 20010906. PRIORITY: US 2000-PV230391 20000906; US 2000-PV255033 20001212.

AB The present invention generally relates to the detection, treatment or prevention of disease states. Specifically, the present invention relates to the detection, treatment or prevention of amyloidosis or amyloid-assocd. diseases. The present invention further comprises methods and compns. comprising therapeutic ***vaccines*** , antisera and mol. constructs, comprising expression vectors and fusion proteins encoded therein. The fusion proteins comprise light chain variable domain of monoclonal antibody 6C6 recognizing . ***beta*** .- ***amyloid*** epitope and capable of solubilizing . ***beta*** .- ***amyloid*** fibers and tangles. The fusion proteins also comprise fragment of transferrin capable of crossing blood brain barrier.

L4 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

2002:127702 Document No. 137:61728 Towards Alzheimer's . ***beta*** .- ***amyloid*** vaccination. Frenkel, Dan; Solomon, Beka (Department of Molecular Microbiology and Biotechnology, Faculty of Life Sciences, Tel-Aviv University, Tel-Aviv, 69978, Israel). Biologicals, 29(3/4), 243-247 (English) 2001. CODEN: BILSEC. ISSN: 1045-1056. Publisher: Academic Press.

AB ***Beta*** - ***amyloid*** pathol., the main hallmark of Alzheimer's disease (AD), has been linked to its conformational status and aggregation. The authors recently showed that site-directed monoclonal antibodies (mAbs) towards the N-terminal region of the human . ***beta*** .- ***amyloid*** peptide bind to preformed . ***beta*** .- ***amyloid*** fibrils (A.beta.), leading to disaggregation and inhibition of their neurotoxic effect. Here the authors report the development of a novel immunization procedure to raise effective anti-aggregating amyloid.beta.-protein (A.beta.P) antibodies, using as antigen filamentous phages displaying the only EFRH peptide the epitope of these antibodies. Due to the high antigenicity of the phage no ***adjuvant*** is required to obtain high affinity anti-aggregating IgG antibodies in animals model, that exhibit identity to human A.beta.P. Such antibodies are able to sequester peripheral A.beta.P, thus avoiding passage through the blood brain barrier (BBB) and, as recently shown in a transgenic mouse model, to cross the BBB and dissolve already formed . ***beta*** .- ***amyloid*** plaques. To the authors' knowledge, this is the first attempt to use as a ***vaccine*** a self-anti-aggregating epitope displayed on a phage, and this may pave the way to treat abnormal accumulation-peptide diseases, such as Alzheimer's disease or other amyloidogenic diseases. (c) 2001 The International Association of Biological Standardization.

L4 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

2002:43677 Document No. 137:4576 Nasal vaccination with . ***beta*** .- ***amyloid*** peptide for the treatment of Alzheimer's disease. Lemere, Cynthia A.; Maron, Ruth; Selkoe, Dennis J.; Weiner, Howard L. (Center for Neurologic Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA). DNA and Cell Biology, 20(11), 705-711 (English) 2001. CODEN: DCEBE8. ISSN: 1044-5498. Publisher: Mary Ann Liebert, Inc..

AB A review with new data. Alzheimer's disease (AD) is a severe neurodegenerative disease for which there is currently no effective prevention or treatment. The prediction that the no. of U.S. patients with AD will triple to approx. 14 million over the next 50 yr underscores the urgent need to explore novel therapeutic strategies for AD. The . ***beta*** .- ***amyloid*** protein (A.beta.) accumulation and accompanying inflammation appear to play key roles in initiating the neuronal degeneration that underlies the signs and symptoms of AD. Interventions geared toward reducing A.beta. accumulation and inflammatory responses should delay or prevent the onset of the clin. disease. Recently, several research groups, including ours, have shown that vaccination with A.beta. results in a significant lowering of the A.beta. burden in the brains of APP transgenic mice and, in some studies,

improvement in their cognitive deficits. Our study described a novel approach, namely mucosal (intranasal) A.beta. vaccination. Precisely how A.beta. vaccination chronically lowers A.beta. levels and reduces A.beta.-assocd. pathol. remains unclear. Here, we provide an overview of these studies, with particular emphasis on our work with intranasal A.beta. vaccination. Examples of other intranasal ***vaccines*** and mucosal ***adjuvants*** are presented. Taken together, these data have implications for the future development of an intranasal A.beta. ***vaccine*** for humans.

L4 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
2001:839097 Document No. 136:339060 Amyloid .beta. peptide as a ***vaccine*** for Alzheimer's disease involves receptor-mediated transport at the blood-brain barrier. Poduslo, Joseph F.; Curran, Geoffry L. (Molecular Neurobiology Laboratory, Departments of Neurology, Neuroscience, Mayo Clinic, Rochester, MN, 55905, USA). NeuroReport, 12(15), 3197-3200 (English) 2001. CODEN: NERPEZ. ISSN: 0959-4965. Publisher: Lippincott Williams & Wilkins.

AB Much research is now focused on a potential ***vaccine*** for Alzheimer's disease (AD). Current studies involve administering the amyloid .beta. peptide (A.beta.) in Freund's complete ***adjuvant*** , which cannot be used in humans. The authors' studies show that the immune complex of A.beta. is taken up by a receptor-mediated process at the blood-brain barrier (BBB). The success of immunization for AD, therefore, may be critically dependent on circulating A.beta. levels which are lower in AD patients compared to AD transgenic mice. Moreover, the authors have found that modifying the antibody with polyamine increases its BBB permeability and may provide a better approach to passive immunization for Alzheimer's disease.

L4 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
2001:635921 Document No. 135:200402 Novel method for down-regulation of amyloid. Birk, Peter; Jensen, Martin Roland; Nielsen, Klaus Gregorius (M + E Biotech A/S, Den.). PCT Int. Appl. WO 2001062284 A2 20010830, 120 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-DK113 20010219. PRIORITY: DK 2000-265 20000221; US 2000-PV186295 20000301.

AB Disclosed are novel methods for combating diseases characterized by deposition of amyloid. The methods generally rely on immunization against amyloidogenic proteins (proteins contributing to formation of amyloid) such as ***beta*** ***amyloid*** (A.beta.). Immunization is preferably effected by administration of analogs of autologous amyloidogenic polypeptides, said analogs being capable of inducing antibody prodn. against the autologous amyloidogenic polypeptides. Esp. preferred as an immunogen is autologous A.beta. which has been modified by introduction of one single or a few foreign, immunodominant and promiscuous T-cell epitopes while substantially preserving the majority of A.beta.'s B-cell epitopes. Also disclosed are nucleic acid vaccination against amyloidogenic polypeptides and vaccination using live ***vaccines*** as well as methods and means useful for the vaccination. Such methods and means include methods for identification of useful immunogenic analogs of the amyloidogenic proteins, methods for the prepn. of analogs and pharmaceutical formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and pharmaceutical formulations.

L4 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN
2001:435132 Document No. 135:60157 Chimeric peptides as immunogens, antibodies thereto, and methods for immunization using chimeric peptides or antibodies. Chain, Benjamin (Mindset Biopharmaceuticals (Usa), Inc., USA). PCT Int. Appl. WO 2001042306 A2 20010614, 47 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,

MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33203 20001208. PRIORITY: US 1999-PV169687 19991208.

AB The invention provides a chimeric peptide or mixt. of chimeric peptides that can be formulated as an immunizing compn. and used in a method for immunization of a mammal against an internal peptide cleavage product derived from a precursor or mature protein, for which the peptide cleavage product and the precursor or mature protein are self mols. The chimeric peptide or peptides have an end-specific B cell epitope from a naturally-occurring internal peptide cleavage product of a precursor or mature protein, as a free N- or C- terminus, fused with or without spacer residues to a T helper cell epitope derived from a living source different from that of the internal peptide cleavage product. The internal peptide cleavage product is an amyloid .beta. peptide derived from cleavage of . ***beta*** . ***amyloid*** precursor protein (.beta.APP); and the chimeric peptide of T helper cell epitope is derived from tetanus toxoid, pertussis toxin, diphtheria toxin, measles virus F protein, etc. Antibodies or monoclonal antibodies raised with the chimeric peptides are useful for passive immunotherapy of diseases such as Alzheimer's disease.

L4 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS on STN

2000:759909 Document No. 134:28316 Immunization against Alzheimer's . ***beta*** .- ***amyloid*** plaques via EFRH phage administration. Frenkel, Dan; Katz, Odelia; Solomon, Beka (Department of Molecular Microbiology and Biotechnology, The George S. Wise Faculty of Life Sciences, Tel-Aviv University, Tel-Aviv, 69978, Israel). Proceedings of the National Academy of Sciences of the United States of America, 97(21), 11455-11459 (English) 2000. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB The epitope EFRH, corresponding to amino acids 3-6 within the human . ***beta*** .- ***amyloid*** peptide (A.beta.P), acts as a regulatory site controlling both the formation and disaggregation process of the . ***beta*** .- ***amyloid*** fibrils (A.beta.). Locking of this epitope by highly specific antibodies affects the dynamics of the entire A.beta.P mol., preventing self-aggregation as well as enabling resolubilization of already formed aggregates. Prodn. of such antibodies by repeated injections of toxic human A.beta. fibrils into transgenic mice suggests the feasibility of vaccination against Alzheimer's disease. Here, the authors report the development of an immunization procedure for the prodn. of effective anti-aggregating . ***beta*** .- ***amyloid*** antibodies based on filamentous phages displaying the EFRH peptide as specific and nontoxic antigen. Effective autoimmune antibodies were obtained by EFRH phage administration in guinea pigs, which exhibit A.beta.P identical to the human A.beta.P region. Moreover, because of the high antigenicity of the phage, no ***adjuvant*** is required to obtain high affinity anti-aggregating IgG antibodies after a short immunization period of 3 wk. Availability of such antibodies opens up possibilities for the development of an efficient and long-lasting vaccination for the prevention and treatment of Alzheimer's disease.

L4 ANSWER 14 OF 18 MEDLINE on STN

2002135863 Document Number: 21840729. PubMed ID: 11851323. Towards Alzheimer's ***beta*** - ***amyloid*** vaccination. Frenkel D; Solomon B. (Department of Molecular Microbiology and Biotechnology, Faculty of Life Sciences, Tel-Aviv University, Ramat Aviv, Tel-Aviv 69978, Israel.) BIOLOGICALS, (2001 Sep-Dec) 29 (3-4) 243-7. Journal code: 9004494. ISSN: 1045-1056. Pub. country: England: United Kingdom. Language: English.

AB ***Beta*** .- ***amyloid*** pathology, the main hallmark of Alzheimer's disease (AD), has been linked to its conformational status and aggregation. We recently showed that site-directed monoclonal antibodies (mAbs) towards the N-terminal region of the human ***beta*** - ***amyloid*** peptide bind to preformed ***beta*** - ***amyloid*** fibrils (Abeta), leading to disaggregation and inhibition of their neurotoxic effect. Here we report the development of a novel immunization procedure to raise effective anti-aggregating amyloid beta-protein (AbetaP) antibodies, using as antigen filamentous phages displaying the only EFRH peptide found to be the epitope of these antibodies. Due to the

high antigenicity of the phage no ***adjuvant*** is required to obtain high affinity anti-aggregating IgG antibodies in animals model, that exhibit identity to human AbetaP. Such antibodies are able to sequester peripheral AbetaP, thus avoiding passage through the blood brain barrier (BBB) and, as recently shown in a transgenic mouse model, to cross the BBB and dissolve already formed ***beta*** - ***amyloid*** plaques. To our knowledge, this is the first attempt to use as a ***vaccine*** a self-anti-aggregating epitope displayed on a phage, and this may pave the way to treat abnormal accumulation-peptide diseases, such as Alzheimer's disease or other amyloidogenic diseases.

L4 ANSWER 15 OF 18 MEDLINE on STN
2002062661 Document Number: 21648352. PubMed ID: 11788048. Nasal vaccination with ***beta*** - ***amyloid*** peptide for the treatment of Alzheimer's disease. Lemere C A; Maron R; Selkoe D J; Weiner H L. (Center for Neurologic Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.. lemere@cnd.bwh.harvard.edu) . DNA AND CELL BIOLOGY, (2001 Nov) 20 (11) 705-11. Journal code: 9004522. ISSN: 1044-5498. Pub. country: United States. Language: English.
AB Alzheimer's disease (AD) is a severe neurodegenerative disease for which there is currently no effective prevention or treatment. The prediction that the number of U.S. patients with AD will triple to approximately 14 million over the next 50 years underscores the urgent need to explore novel therapeutic strategies for AD. The ***beta*** - ***amyloid*** protein (Abeta) accumulation and accompanying inflammation appear to play key roles in initiating the neuronal degeneration that underlies the signs and symptoms of AD. Interventions geared toward reducing Abeta accumulation and inflammatory responses should delay or prevent the onset of the clinical disease. Recently, several research groups, including ours, have shown that vaccination with Abeta results in a significant lowering of the Abeta burden in the brains of APP transgenic mice and, in some studies, improvement in their cognitive deficits. Our study described a novel approach, namely mucosal (intranasal) Abeta vaccination. Precisely how Abeta vaccination chronically lowers Abeta levels and reduces Abeta-associated pathology remains unclear. Here, we provide an overview of these studies, with particular emphasis on our work with intranasal Abeta vaccination. Examples of other intranasal ***vaccines*** and mucosal ***adjuvants*** are presented. Taken together, these data have implications for the future development of an intranasal Abeta ***vaccine*** for humans.

L4 ANSWER 16 OF 18 MEDLINE on STN
2001664462 Document Number: 21568466. PubMed ID: 11711855. Amyloid beta peptide as a ***vaccine*** for Alzheimer's disease involves receptor-mediated transport at the blood-brain barrier. Poduslo J F; Curran G L. (Molecular Neurobiology Laboratory, Department of Neurology, Mayo Clinic, Rochester, MN 55905, USA.) NEUROREPORT, (2001 Oct 29) 12 (15) 3197-200. Journal code: 9100935. ISSN: 0959-4965. Pub. country: England: United Kingdom. Language: English.
AB Much research is now focused on a potential ***vaccine*** for Alzheimer's disease (AD). Current studies involve administering the amyloid beta peptide (Abeta) in Freund's complete ***adjuvant*** , which cannot be used in humans. Our studies show that the immune complex of Abeta is taken up by a receptor-mediated process at the blood-brain barrier (BBB). The success of immunization for AD, therefore, may be critically dependent on circulating Abeta levels which are lower in AD patients compared to AD transgenic mice. Moreover, we have found that modifying the antibody with polyamine increases its BBB permeability and may provide a better approach to passive immunization for Alzheimer's disease.

L4 ANSWER 17 OF 18 MEDLINE on STN
2001521120 Document Number: 21451777. PubMed ID: 11569944. AN-1792 (Elan). Thatte U. (Seth GS Medical College, Department of Pharmacology and Therapeutics, Parel, Mumbai, India.. mthatte@bom5.vsnl.net.in) . Curr Opin Investig Drugs, (2001 May) 2 (5) 663-7. Ref: 27. Journal code: 100965718. ISSN: 1472-4472. Pub. country: England: United Kingdom. Language: English.
AB Elan is developing AN-1792 as a potential immunotherapy for Alzheimer's disease (AD). It is currently in phase I trials [350904]. Phase II/III

trials, running in parallel in the US and UK, are expected to start by the end of 2001 [375061], [383226], [401966]. American Home Products (AHP) are collaborating with Elan on research and development of an immunotherapy directed towards the ***beta*** - ***amyloid*** peptide, including AN-1792 and other potential products [361702]. In September 2000, an agreement was established between Elan, AHP and Cambridge Antibody Technology (CAT), whereby CAT are investigating anti-***beta*** - ***amyloid*** human antibodies [394844]. In July 2000, Merrill Lynch predicted a possible late-2001 entry into pivotal trials with a potential NDA filing in 2004 [375966]. The clinical program is expected to take approximately four years [339630]. In April 2001, ABN Amro Hoare Govett stated that, if data from the large phase II trial expected to start late in 2001 satisfied FDA requirements, then Elan might be able to file an NDA in 2003, with a potential launch in 2005 [407412].

L4 ANSWER 18 OF 18 MEDLINE on STN
95323549 Document Number: 95323549. PubMed ID: 7600179. Hypothesis: is Alzheimer's disease a metal-induced immune disorder?. Armstrong R A; Winsper S J; Blair J A. (Aston University, Birmingham.)
NEURODEGENERATION, (1995 Mar) 4 (1) 107-11. Journal code: 9209022. ISSN: 1055-8330. Pub. country: ENGLAND: United Kingdom. Language: English.
AB A hypothesis that a metal-induced immune disorder may be involved in the pathogenesis of some forms of Alzheimer's disease (AD) is presented. The classical complement pathway is activated in AD and T cells and reactive microglia appear in the brain. Studies of metal induced autoimmunity and the use of compounds containing aluminium as ***vaccine*** ***adjuvants*** suggest that metals can activate complement and can be taken up by antigen presenting cells. The consequent immune response could contribute to neuronal damage, ***beta*** - ***amyloid*** deposition and cell death. The strengths and weaknesses of this hypothesis are discussed and tests of some aspects are proposed.

=> S ANTIBODY
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L6 14 L3 NOT L4

=> D 1-14 CBIB ABS

L6 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
2003:467767 Subacute meningoencephalitis in a subset of patients with AD after A.beta.42 immunization. Orgogozo, J.-M.; Gilman, S.; Dartigues, J.-F.; Laurent, B.; Puel, M.; Kirby, L. C.; Jouanny, P.; Dubois, B.; Eisner, L.; Flitman, S.; Michel, B. F.; Boada, M.; Frank, A.; Hock, C. (Saint-Etienne, CHU Bellevue, Department of Neurology and Neurogeriatrics (Dr. Laurent), University of Bordeaux, and Neuroepidemiology Research Unit, CHU Pellegrin, Federation of Neurology (Drs. Orgogozo and Dartigues), Neurology Federation and Geriatric Department (Dr. Puel), France, INSERM U-330, Switz.). Neurology, 61(1), 46-54 (English) 2003. CODEN: NEURAI. ISSN: 0028-3878. Publisher: Lippincott Williams & Wilkins.
AB Background: AD is characterized by cerebral deposition of . ***beta*** .- ***amyloid*** plaques with amyloid .beta.-peptide (A.beta.) 42 as the major peptide constituent, along with neurofibrillary tangles and neuronal loss. In transgenic mice, active immunization against A.beta.42 removes these plaques and improves cognitive function. A Phase I study in AD patients demonstrated good safety and tolerability of multiple injections of aggregated A.beta.42 (AN1792) with QS-21 as ***adjuvant*** . Methods: Three hundred seventy-two patients with mild to moderate AD were randomized to receive IM injections of AN1792 or placebo (4:1) at baseline and at months 1, 3, 6, 9, and 12 in a multicenter Phase II safety, tolerability, and pilot efficacy study. Dosing was terminated after four early reports of meningoencephalitis, but follow-up continued. The study remains blinded, and further results will be reported after its termination. Results: Symptoms and lab. findings consistent with meningoencephalitis occurred in 18 of 298 (6%) patients treated with AN1792 compared with 0 of 74 on placebo ($p = 0.020$). Sixteen of the 18 had received two doses, one had received one dose, and one had received three doses of the study drug before symptoms occurred. The median latency from the first and last injections to symptoms was 75 and 40 days.

No case occurred later than 6 mo after the first immunization. Anti-A.beta.42 antibody titers were not correlated with the occurrence or severity of symptoms or relapses. Twelve patients recovered to or close to baseline within weeks, whereas six remain with disabling cognitive or neurol. sequelae. All 18 patients remain alive to date (Dec. 31, 2002), 6 mo to >1 yr after symptom onset. Conclusions: Postvaccination meningoencephalitis occurred without clear relation to serum anti-A.beta.42 antibody titers. Potential mechanisms such as T-cell and microglial activation may be responsible and are under consideration to develop a safer anti-A.beta. immunotherapy for AD.

L6 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

2003:325037 Document No. 139:51289 ***Adjuvant*** -dependent modulation of Th1 and Th2 responses to immunization with . ***beta*** .-***amyloid*** . Cribbs, David H.; Ghochikyan, Anahit; Vasilevko, Vitaly; Tran, Mike; Petrushina, Irina; Sadzikava, Nadya; Babikyan, Davit; Kesslak, Patrick; Kieber-Emmons, Thomas; Cotman, Carl W.; Agadjanyan, Michael G. (Institute for Brain Aging and Dementia, University of California Irvine, Irvine, CA, 92697-4540, USA). International Immunology, 15(4), 505-514 (English) 2003. CODEN: INIMEN. ISSN: 0953-8178. Publisher: Oxford University Press.

AB The role of ***adjuvant*** on the Th1 and Th2 immune responses to A.beta.-immunotherapy (A.beta.42peptide) was examd. in wild-type mice. Fine epitope anal. with overlapping oligomers of the A.beta.42 sequence identified the 1-15 region as a dominant B cell epitope. The 6-20 peptide was recognized only weakly by antisera from mice administrated with A.beta.42 peptide formulated in complete Freund's ***adjuvant*** (CFA), alum or TiterMax Gold (TMG). However, mice immunized with A.beta.42 mixed with QS21 induced a significant antibody response to the 6-20 peptide. The only T cell epitope found was within the 6-28 sequence of A.beta.42. QS21 and CFA induced the strongest humoral response to A.beta., alum was intermediate, and TMG the weakest ***adjuvant*** . Anal. of antibody isotypes specific for A.beta. indicates that alum induces primarily Th2-type immune response, whereas TMG, CFA and QS21 shift the immune responses toward a Th1 phenotype. Stimulation of splenocytes from A.beta.-immunized mice with A.beta.40 peptide induced strikingly different cytokine expression profiles. QS21 and CFA induced significant IFN-.gamma., IL-4 and tumor necrosis factor-.alpha. expression, whereas alum induced primarily IL-4 prodn. As Th1-type immune responses have been implicated in many autoimmune disorders, whereas Th2-type responses have been shown to inhibit autoimmune disease, the choice of ***adjuvant*** may be crit. for the design of a safe and effective immunotherapy for Alzheimer's disease.

L6 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN

2003:311611 A.beta.1-15 is less immunogenic than A.beta.1-40/42 for intranasal immunization of wild-type mice but may be effective for "boosting". Leverone, Jodi F.; Spooner, Edward T.; Lehman, Herman K.; Clements, John D.; Lemere, Cynthia A. (Harvard Institutes of Medicine 622, Center for Neurologic Diseases, Department of Neurology, Brigham and Women's Hospital, Boston, MA, 021155716, USA). Vaccine, 21(17-18), 2197-2206 (English) 2003. CODEN: VACCDE. ISSN: 0264-410X. Publisher: Elsevier Science Ltd..

AB Immunizing mouse models of Alzheimer's disease (AD) against . ***beta*** .- ***amyloid*** (A.beta.) leads to a decrease in cerebral A.beta. burden as well as an improvement in behavioral deficits. Circulating A.beta.-antibodies may be responsible for interfering with A.beta. deposition. In the present study, we attempted to initiate more robust antibody prodn. in wild type (WT) mice. Three immunization strategies were examd.: intranasal (i.n.) immunization with A.beta.1-15 or full-length A.beta.1-40/42, i.n. administration of A.beta. combined with mucosal ***adjuvants*** , native labile enterotoxin (LT) or its non-toxic form, LT(R192G), and prime-boost regimes. Using A.beta.1-15 as the primary immunogen for intranasal immunization did not initiate strong antibody prodn. When A.beta.1-15 or A.beta.1-40/42 was combined with native LT or LT(R192G), antibody prodn. was significantly increased. Nasal immunization with A.beta.1-15 and native LT successfully "boosted" an immune response "primed" by an i.p. injection of A.beta.1-40/42, producing moderately high A.beta. titers that remained stable for at least 6 mo. Serum anti-A.beta. antibodies, regardless of the length of the A.beta. immunogen, consistently detected human AD plaques, had epitopes

within A.beta.1-15, and were predominantly of the IgG2b, IgG1, and IgG2a isotypes. The ***adjuvants*** were well-tolerated in the mice. Thus, A.beta.1-15 may have potential as a safer, more cost-effective "boosting" immunogen than the full-length A.beta. peptide for chronic, active A.beta. immunization.

L6 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
2001:520215 Document No. 136:374687 Encapsulation in biodegradable microparticles enhances serum antibody response to parenterally-delivered . ***beta*** .- ***amyloid*** in mice. Brayden, D. J.; Templeton, L.; McClean, S.; Barbour, R.; Huang, J.; Nguyen, M.; Ahern, D.; Motter, R.; Johnson-Wood, K.; Vasquez, N.; Schenk, D.; Seubert, P. (Biotechnology Building, Elan Biotechnology Research, Trinity College, Dublin, Ire.). Vaccine, 19(30), 4185-4193 (English) 2001. CODEN: VACCDE. ISSN: 0264-410X. Publisher: Elsevier Science Ltd..
AB Poly(lactide-co-glycolide) (PLG) microspheres were tested as a parenteral delivery system for human . ***beta*** .- ***amyloid*** (1-42) (A.beta.), a potential immunotherapeutic undergoing assessment in Phase 1 studies for Alzheimer's disease (AD). A.beta. was successfully encapsulated in PLG microspheres of av. sizes of 3 or 15 .mu.m diam. Swiss Webster (SW) mice were injected by the sub-cutaneous (s.c.) or intra-peritoneal (i.p.) routes with 3-33 .mu.g A.beta.. A.beta.-PLG microparticles (3 .mu.m) induced dose-dependent antibody responses, which were maximal at 33 .mu.g A.beta., while A.beta. in phosphate-buffered saline (PBS) produced weak antibody responses at the same doses by both routes. Significantly increased antibody responses were seen for both small and large particle formulations given by the i.p. route in comparison to the s.c route. It was previously reported that passive immunization with A.beta.-specific antibodies cleared amyloid plaques in a mouse model of AD, an indication that induction of serum antibody is a prerequisite for efficacy.

L6 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2003 ACS on STN
2000:861510 Document No. 134:32983 Compositions of A.beta. peptide and processes for producing same. Hirtzer, Pamela; Patel, Naina (Neuralab, Ltd., Bermuda). PCT Int. Appl. WO 2000072870 A1 20001207, 49 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US15302 20000601. PRIORITY: US 1999-PV137047 19990601.
AB The invention is directed to compns. comprising solubilized A.beta. peptide or suspension of A.beta. peptide and to processes for producing the same by adjusting the pH sufficient to effect the solubilization, and sterile filtration thereof, to methods of treating and preventing Alzheimer's disease with the obtained compns.

L6 ANSWER 6 OF 14 MEDLINE on STN
2003188890 Document Number: 22593982. PubMed ID: 12706711. Abeta1-15 is less immunogenic than Abeta1-40/42 for intranasal immunization of wild-type mice but may be effective for "boosting". Leverone Jodi F; Spooner Edward T; Lehman Herman K; Clements John D; Lemere Cynthia A. (Department of Neurology, Center for Neurologic Diseases, Harvard Institutes of Medicine 622, Brigham and Women's Hospital, 77 Avenue Louis Pasteur, 021155716, Boston, MA, USA.) VACCINE, (2003 May 16) 21 (17-18) 2206-15. Journal code: 8406899. ISSN: 0264-410X. Pub. country: Netherlands. Language: English.
AB Immunizing mouse models of Alzheimer's disease (AD) against ***beta*** - ***amyloid*** (Abeta) leads to a decrease in cerebral Abeta burden as well as an improvement in behavioral deficits. Circulating Abeta-antibodies may be responsible for interfering with Abeta deposition. In the present study, we attempted to initiate more robust antibody production in wild type (WT) mice. Three immunization strategies were examined: intranasal (i.n.) immunization with Abeta1-15 or full-length Abeta1-40/42, i.n. administration of Abeta combined with mucosal ***adjuvants*** , native labile enterotoxin (LT) or its non-toxic form,

LT(R192G), and prime-boost regimes. Using Abeta1-15 as the primary immunogen for intranasal immunization did not initiate strong antibody production. When Abeta1-15 or Abeta1-40/42 was combined with native LT or LT(R192G), antibody production was significantly increased. Nasal immunization with Abeta1-15 and native LT successfully "boosted" an immune response "primed" by an intraperitoneal (i.p.) injection of Abeta1-40/42, producing moderately high Abeta titers that remained stable for at least 6 months. Serum anti-Abeta antibodies, regardless of the length of the Abeta immunogen, consistently detected human AD plaques, had epitopes within Abeta1-15, and were predominantly of the IgG2b, IgG1, and IgG2a isotypes. The ***adjuvants*** were well-tolerated in the mice. Thus, Abeta1-15 may have potential as a safer, more cost-effective "boosting" immunogen than the full-length Abeta peptide for chronic, active Abeta immunization.

L6 ANSWER 7 OF 14 MEDLINE on STN

2003184185 Document Number: 22549518. PubMed ID: 12663680.

Adjuvant -dependent modulation of Th1 and Th2 responses to immunization with ***beta*** - ***amyloid*** . Cribbs David H; Ghochikyan Anahit; Vasilevko Vitaly; Tran Mike; Petrushina Irina; Sadzikava Nadya; Babikyan Davit; Kesslak Patrick; Kieber-Emmons Thomas; Cotman Carl W; Agadjanyan Michael G. (Institute for Brain Aging and Dementia, University of California Irvine, Irvine, CA 92697-4540, USA.) INTERNATIONAL IMMUNOLOGY, (2003 Apr) 15 (4) 505-14. Journal code: 8916182. ISSN: 0953-8178. Pub. country: England: United Kingdom. Language: English.

AB The role of ***adjuvant*** on the T(h)1 and T(h)2 immune responses to Abeta-immunotherapy (Abeta(42)peptide) was examined in wild-type mice. Fine epitope analysis with overlapping oligomers of the Abeta(42) sequence identified the 1-15 region as a dominant B cell epitope. The 6-20 peptide was recognized only weakly by antisera from mice administrated with Abeta(42) peptide formulated in complete Freund's ***adjuvant*** (CFA), alum or TiterMax Gold (TMG).. However, mice immunized with Abeta(42) mixed with QS21 induced a significant antibody response to the 6-20 peptide. The only T cell epitope found was within the 6-28 sequence of Abeta(42). QS21 and CFA induced the strongest humoral response to Abeta, alum was intermediate, and TMG the weakest ***adjuvant*** . Analysis of antibody isotypes specific for Abeta indicates that alum induces primarily T(h)2-type immune response, whereas TMG, CFA and QS21 shift the immune responses toward a T(h)1 phenotype. Stimulation of splenocytes from Abeta-immunized mice with Abeta(40) peptide induced strikingly different cytokine expression profiles. QS21 and CFA induced significant IFN-gamma, IL-4 and tumor necrosis factor-alpha expression, whereas alum induced primarily IL-4 production. As T(h)1-type immune responses have been implicated in many autoimmune disorders, whereas T(h)2-type responses have been shown to inhibit autoimmune disease, the choice of ***adjuvant*** may be critical for the design of a safe and effective immunotherapy for Alzheimer's disease.

L6 ANSWER 8 OF 14 MEDLINE on STN

2003092449 Document Number: 22492151. PubMed ID: 12603286. CSF tau protein and ***beta*** - ***amyloid*** (1-42) in Alzheimer's disease diagnosis: discrimination from normal ageing and other dementias in the Greek population. Kapaki E; Paraskevas G P; Zalonis I; Zournas C. (Department of Neurology, Athens National University, Aeginition Hospital, Athens, Greece.. ekapaki@med.uoa.gr) . EUROPEAN JOURNAL OF NEUROLOGY, (2003 Mar) 10 (2) 119-28. Journal code: 9506311. ISSN: 1351-5101. Pub. country: England: United Kingdom. Language: English.

AB Cerebrospinal fluid (CSF) levels of tau protein and amyloid beta(1-42) peptide (Abeta42) have been suggested as possible diagnostic markers of Alzheimer's disease (AD). In order to evaluate their diagnostic potential in clinical practice, we measured tau and Abeta42 levels in the CSF of 49 AD patients, 15 patients with non-AD neurodegenerative dementias (NAND), six patients with vascular dementia (VD) and 49 elderly controls. All the subjects were of Greek origin. A marked increase in tau, a decrease in Abeta42 and a marked increase in the tau/Abeta42 ratio was noted in AD. Abeta42 alone had a specificity of 80% and a sensitivity of 82% in differentiating AD from normal ageing, whilst the corresponding values for differentiating AD from NAND or VD were 80 and 71, or 67 and 82%, respectively. Tau was better in differentiating AD, from normal ageing (specificity 96%, sensitivity 88%), NAND (specificity 93%, sensitivity

71%) and VD (specificity 83%, sensitivity 94%). The tau/Abeta42 ratio achieved values comparable or even better than tau for differentiating AD from normal ageing (specificity 86%, sensitivity 96%) and VD (specificity 83%, sensitivity 90%) and definitely better than any of the candidate markers alone, for differentiating AD from NAND (specificity 100%, sensitivity 71%). Thus, the combined use of CSF tau and Abeta42 in the form of the tau/Abeta42 ratio is a simple, safe and useful ***adjuvant*** to clinical criteria for dementia diagnosis.

L6 ANSWER 9 OF 14 MEDLINE on STN

2002480127 Document Number: 22226782. PubMed ID: 12242310. Age-related differences in the immune response to immunization with human Abeta42 peptide. Pifer Jeannette; Hennes Jason L; Lee John M; Witte Pamela L. (Departments of Cell Biology, Neurobiology, & Anatomy, Pathology, Loyola University Medical Center, Maywood, Illinois 60153, USA.) JOURNALS OF GERONTOLOGY. SERIES A, BIOLOGICAL SCIENCES AND MEDICAL SCIENCES, (2002 Oct) 57 (10) B355-8. Journal code: 9502837. ISSN: 1079-5006. Pub. country: United States. Language: English.

AB Several studies show that plaque burden is resolved in young to middle-aged amyloid precursor protein transgenic mice after rigorous immunization with Abeta42 peptide. We determined if wild-type 20-month-old and 3-month-old animals could produce high-titer antibody against Abeta42 with a less strenuous immunization protocol. All treated young animals mounted a high-titer (20,000-50,000) response after two immunizations and sustained a strong response for 6 months following the initial treatment with Abeta42. However, 6 of 8 immunized aged animals did not respond after three immunizations. The 2 responding aged mice produced low-titer antibody (5,000-10,000), which rapidly declined to control levels within 5 weeks after the third immunization. Aged animals may require alternate strategies for successful vaccination, such as inclusion of stimulatory cytokines or better ***adjuvants*** . If tolerance to Abeta42 underlies the poor response observed in aged animals, then a mechanism to overcome this response will have to be investigated.

L6 ANSWER 10 OF 14 MEDLINE on STN

2002190395 Document Number: 21920996. PubMed ID: 11923407. Noradrenergic depletion potentiates ***beta*** - ***amyloid*** -induced cortical inflammation: implications for Alzheimer's disease. Heneka Michael T; Galea Elena; Gavriluyk Vitaliy; Dumitrescu-Ozimek Lucia; Daeschner JoAnna; O'Banion M Kerry; Weinberg Guy; Klockgether Thomas; Feinstein Douglas L. (Department of Neurology, University of Bonn, Germany 53127.) JOURNAL OF NEUROSCIENCE, (2002 Apr 1) 22 (7) 2434-42. Journal code: 8102140. ISSN: 1529-2401. Pub. country: United States. Language: English.

AB Degeneration of locus ceruleus (LC) neurons and reduced levels of norepinephrine (NE) in LC projection areas are well known features of Alzheimer's disease (AD); however, the consequences of those losses are not clear. Because inflammatory mediators contribute to AD pathogenesis and because NE can suppress inflammatory gene expression, we tested whether LC loss influenced the brain inflammatory gene expression elicited by amyloid beta (Abeta). Adult rats were injected with the selective neurotoxin N-(2-chloroethyl)-N-ethyl-2 bromobenzylamine (DSP4) to induce LC death and subsequently injected in the cortex with Abeta (aggregated 1-42 peptide). DSP4 treatment potentiated the Abeta-dependent induction of inflammatory nitric oxide synthase (iNOS), interleukin (IL)-1beta, and IL-6 expression compared with control animals. In contrast, the induction of cyclooxygenase-2 expression was not modified by DSP4 treatment. In control animals, injection of Abeta induced iNOS primarily in microglial cells, whereas in DSP4-treated animals, iNOS was localized to neurons, as is observed in AD brains. Injection of Abeta increased IL-1beta expression initially in microglia and at later times in astrocytes, and expression levels were greater in DSP4-treated animals than in controls. The potentiating effects of DSP4 treatment on iNOS and IL-1beta expression were attenuated by coinjection with NE or the beta-adrenergic receptor agonist isoproterenol. These data demonstrate that LC loss and NE depletion augment inflammatory responses to Abeta and suggest that LC loss in AD is permissive for increased inflammation and neuronal cell death.

L6 ANSWER 11 OF 14 MEDLINE on STN

2001532660 Document Number: 21463445. PubMed ID: 11578773. Immunological aspects of microglia: relevance to Alzheimer's disease. Benveniste E N; Nguyen V T; O'Keefe G M. (Department of Cell Biology, The University of

Alabama at Birmingham, 1918 University Boulevard, MCLM 395, Birmingham, AL 35294-0005, USA.. tika@uab.edu) . NEUROCHEMISTRY INTERNATIONAL, (2001 Nov-Dec) 39 (5-6) 381-91. Ref: 124. Journal code: 8006959. ISSN: 0197-0186. Pub. country: England: United Kingdom. Language: English.

AB Alzheimer's disease (AD) is a progressive dementing neurologic illness, and the most frequent cause of dementia in the elderly. Neuritic plaques are one of the main neuropathological findings in AD, and the major protein component is the ***beta*** - ***amyloid*** protein (A beta). Another striking feature of neuritic plaques is the presence of activated microglia, cytokines, and complement components, suggestive of "inflammatory foci" within AD brain. In this review, we will examine the mechanisms by which microglia become activated in AD, emphasizing the role in the A beta protein and proinflammatory cytokines. As well, pathways for suppression of microglial activation by immunosuppressive cytokines will be described. Inflammation mediated by activated microglia is an important component of AD pathophysiology, and strategies to control this response could provide new therapeutic approaches for the treatment of AD.

L6 ANSWER 12 OF 14 MEDLINE on STN

2001022669 Document Number: 20481929. PubMed ID: 11027345. Immunization against Alzheimer's ***beta*** - ***amyloid*** plaques via EFRH phage administration. Frenkel D; Katz O; Solomon B. (Department of Molecular Microbiology and Biotechnology, The George S. Wise Faculty of Life Sciences, Tel-Aviv University, Ramat Aviv, Tel-Aviv 69978, Israel.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2000 Oct 10) 97 (21) 11455-9. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The epitope EFRH, corresponding to amino acids 3-6 within the human ***beta*** - ***amyloid*** peptide (AbetaP), acts as a regulatory site controlling both the formation and disaggregation process of the ***beta*** - ***amyloid*** fibrils (Abeta). Locking of this epitope by highly specific antibodies affects the dynamics of the entire AbetaP molecule, preventing self-aggregation as well as enabling resolubilization of already formed aggregates. Production of such antibodies by repeated injections of toxic human Abeta fibrils into transgenic mice suggests the feasibility of vaccination against Alzheimer's disease. Here, we report the development of an immunization procedure for the production of effective anti-aggregating ***beta*** - ***amyloid*** antibodies based on filamentous phages displaying the EFRH peptide as specific and nontoxic antigen. Effective autoimmune antibodies were obtained by EFRH phage administration in guinea pigs, which exhibit AbetaP identical to the human AbetaP region. Moreover, because of the high antigenicity of the phage, no ***adjuvant*** is required to obtain high affinity anti-aggregating IgG antibodies after a short immunization period of 3 weeks. Availability of such antibodies opens up possibilities for the development of an efficient and long-lasting vaccination for the prevention and treatment of Alzheimer's disease.

L6 ANSWER 13 OF 14 MEDLINE on STN

2000133621 Document Number: 20133621. PubMed ID: 10668442. Protective and rescuing abilities of IGF-I and some putative free radical scavengers against ***beta*** - ***amyloid*** -inducing toxicity in neurons. Dore S; Bastianetto S; Kar S; Quirion R. (Douglas Hospital Research Center, McGill University, Montreal, Quebec, Canada.) ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1999) 890 356-64. Journal code: 7506858. ISSN: 0077-8923. Pub. country: United States. Language: English.

AB ***beta*** - ***Amyloid*** (A beta) peptides are most likely involved in the neurodegenerative process occurring in Alzheimer's Disease (AD) and are enriched in senile plaques. The mechanisms of A beta toxicity are not clear but likely involve free radicals and apoptosis. Much interest is currently aiming at developing effective approaches to block A beta toxicity in order to slow down disease progression. In that context, we are particularly interested in studying the role of insulin-like growth factors, particularly IGF-I and purported free radical scavengers including a Gingko biloba extract (EGb761) as blocker of A beta toxicity in a simple in vitro model of hippocampal primary cultures. We observed that both IGF-I and EGb761 are unique in that they are able not only to protect but even to rescue neurons against A beta toxicity. These results are summarized here and possible mechanisms of action are discussed to explain the protective properties of these two classes of agents.

L6 ANSWER 14 OF 14 MEDLINE on STN
1999334930 Document Number: 99334930. PubMed ID: 10408445. Immunization with amyloid-beta attenuates Alzheimer-disease-like pathology in the PDAPP mouse. Schenk D; Barbour R; Dunn W; Gordon G; Grajeda H; Guido T; Hu K; Huang J; Johnson-Wood K; Khan K; Kholodenko D; Lee M; Liao Z; Lieberburg I; Motter R; Mutter L; Soriano F; Shopp G; Vasquez N; Vandevert C; Walker S; Wogulis M; Yednock T; Games D; Seubert P. (Elan Pharmaceuticals, South San Francisco, California 94080, USA.. dschenk@elanpharma.com) . NATURE, (1999 Jul 8) 400 (6740) 173-7. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Amyloid-beta peptide (Abeta) seems to have a central role in the neuropathology of Alzheimer's disease (AD). Familial forms of the disease have been linked to mutations in the amyloid precursor protein (APP) and the presenilin genes. Disease-linked mutations in these genes result in increased production of the 42-amino-acid form of the peptide (Abeta42), which is the predominant form found in the amyloid plaques of Alzheimer's disease. The PDAPP transgenic mouse, which overexpresses mutant human APP (in which the amino acid at position 717 is phenylalanine instead of the normal valine), progressively develops many of the neuropathological hallmarks of Alzheimer's disease in an age- and brain-region-dependent manner. In the present study, transgenic animals were immunized with Abeta42, either before the onset of AD-type neuropathologies (at 6 weeks of age) or at an older age (11 months), when amyloid-beta deposition and several of the subsequent neuropathological changes were well established. We report that immunization of the young animals essentially prevented the development of ***beta*** - ***amyloid*** -plaque formation, neuritic dystrophy and astrogliosis. Treatment of the older animals also markedly reduced the extent and progression of these AD-like neuropathologies. Our results raise the possibility that immunization with amyloid-beta may be effective in preventing and treating Alzheimer's disease.

=> E RASO/AU
=> S E62,E64-E66
L7 76 ("RASO V"/AU OR "RASO VIC"/AU OR "RASO VICTOR"/AU OR "RASO VICTO R A"/AU)

=> S L7 AND L1
L8 1 L7 AND L1

=> D CBIB ABS

L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
2000:769003 Document No. 133:320995 Anti-idiotype ***vaccines*** to elicit catalytic antibodies. ***Raso, Victor*** ; Paulus, Henry (Boston Biomedical Research Institute, USA). U.S. US 6140091 A 20001031, 28 pp. (English). CODEN: USXXAM. APPLICATION: US 1998-102451 19980622. PRIORITY: US 1997-PV50388 19970620.

AB Disclosed are methods for the prodn. of second generation catalytic antibodies. The method comprises (a) immunizing a first animal with a transition state analog, producing hybridomas and screening for prodn. of monoclonal antibodies specific for the transition state analog and having catalytic activity; (b) immunizing a second animal with the monoclonal antibody identified in step (b) and producing hybridomas and screening for prodn. of anti-idiotic monoclonal antibodies having a structure which mimics the transition state analog; and (c) immunizing a third animal with the anti-idiotypic monoclonal antibody to produce anti-anti-idiotypic antibodies having catalytic activity. The disclosed methods offer a variety of advantages relative to prior art techniques. For example, the methods of the present invention do not require prior identification of the active site of an enzyme, the activity of which is desired in the catalytic antibody. Addnl., the disclosed methods enable the prodn. of antibodies which catalyze chem. reactions which do not occur in nature. The methods are exemplified by the prodn. of catalytic antibodies specific for the transition state adopted by cocaine during chem. hydrolysis.

=> S L7 AND L3
L9 0 L7 AND L3

=> S ADJUVANT·
L10 101103 ADJUVANT

=> S AMYLOID
L11 38186 AMYLOID

=> S L10 AND L11
L12 169 L10 AND L11

=> S L12 AND L1
L13 53 L12 AND L1

=> S L13 NOT L4
L14 35 L13 NOT L4

=> D 1-35 CBIB ABS

L14 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2003:570522 Document No. 139:132440 ***Vaccines*** comprising immunogenic domains of hepatitis B virus core antigen and T or B cell epitopes derived from pathogenic antigen. Birkett, Ashley J. (USA). U.S. Pat. Appl. Publ. US 2003138769 A1 20030724, 131 pp., Cont.-in-part of U.S. Provisional Ser. No. 226,867. (English). CODEN: USXXCO. APPLICATION: US 2001-930915 20010815. PRIORITY: US 2000-PV225843 20000816; US 2000-PV226867 20000822.

AB A chimeric, carboxy-terminal truncated hepatitis B virus nucleocapsid protein (HBc) is disclosed that is engineered for both enhanced stability of self-assembled particles and the display of an immunogenic epitope. The display of the immunogenic epitope is displayed in the immunogenic loop of HBc, whereas the enhanced stability of self-assembled particles is obtained by the presence of at least one heterologous cysteine residue near the carboxy-terminus of the chimer mol. Methods of making and using the chimers are also disclosed. The chimeric proteins also comprise B cell epitope or T cell epitope present in a pathogen such as Streptococcus pneumonia, Cryptosporidum parvum, HIV, foot and mouth disease virus, influenza virus, Yersinia pestis, Haemophilus influenzae, Moraxella catarrhalis, Porphyromonas gingivalis, Trypanosoma cruzi, Plasmodium falciparum, Plasmodium vivax, Plasmodium berghei, Plasmodium yoelii, Streptococcus sobrinus, Shigella flexneri, RSV, Plasodium entamoeba histolytica, Schistosoma japonicum, Schistosoma mansoni, bovine inhibin and ebola virus.

L14 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2003:490996 Document No. 139:67779 Fusion proteins comprising an isolated pathogen associated molecule pattern and an immunostimulatory portion of an antigen for use as ***vaccines*** . Medzhitov, Ruslan; Kopp, Elizabeth (Yale University, USA). PCT Int. Appl. WO 2003051305 A2 20030626, 99 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US40046 20021213. PRIORITY: US 2001-PV340174 20011214.

AB The present invention provides novel ***vaccines*** , methods for the prodn. of such ***vaccines*** and methods of using such ***vaccines*** . The ***vaccines*** comprise chimeric protein of a pathogen assocd. mol. pattern (PAMP) and a antigenic epitope. The PAMPs are targets of innate immune recognition, e.g. chaperone, FimC; and the antigenic epitope is derived from pathogen antigen, tumor antigen, allergen, neural defect-related antigen, cardiovascular disease, rheumatoid arthritis-related antigen, hormone, pregnancy-related antigen, embryonic antigen or fetal antigen. The novel ***vaccines*** of the present invention combine both of the signals necessary to activate native T-cells-a specific antigen and the co-stimulatory signal-leading to a robust and specific T-cell immune response.

L14 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2003:434266 Document No. 139:21013 Synthetic immunogenic/non-deposit-forming polypeptides and peptides homologous to ***amyloid*** .beta., prion protein, amylin, .alpha.-synuclein, or polyglutamine repeats for induction of an immune response. Frangione, Blas; Wisniewski, Thomas; Sigurdsson, Einar M. (New York University, USA). PCT Int. Appl. WO 2003045128 A2 20030605, 265 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US37634 20021121. PRIORITY: US 2001-PV331801 20011121.

AB The present invention relates to immunogenic but non-depositing-forming polypeptides or peptides homologous to ***amyloid*** .beta., prion, amylin or .alpha.-synuclein which can be used alone or conjugated to an immunostimulatory mol. in an immunizing compn. for inducing an immune response to ***amyloid*** .beta. peptides and ***amyloid*** deposits, to prion protein and prion deposits, to amylin and amylin deposits, to .alpha.-synuclein and deposits contg. .alpha.-synuclein, or to polyglutamine repeats and deposits of proteins contg. polyglutamine repeats. Described are also antibodies directed against such peptides, their generation, and their use in methods of passive immunization to such peptides and deposits. These immunogenic polypeptides and antibodies against them are useful for treating diseases such as amyloidosis, Alzheimer's disease, prionoses, type 2 diabetes or islet amyloidosis, Parkinson's disease, and Huntington's disease.

L14 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2003:276663 Document No. 138:302632 ***Adjuvant*** compns. and uses thereof in ***vaccines*** . Friede, Martin; Garcon, Nathalie; Gerard, Catherine Marie Ghislaine; Hermand, Philippe (Smithkline Beecham Biologicals S.A., Belg.). U.S. US 6544518 B1 20030408, 29 pp., Cont.-in-part of Appl. No. PCT/EP00/02920. (English). CODEN: USXXAM. APPLICATION: US 2000-690921 20001018. PRIORITY: GB 1999-8885 19990419; US 1999-301829 19990429; WO 2000-EP2920 20000404.

AB The present invention relates to ***adjuvant*** compns. which are suitable to be used in ***vaccines*** . In particular, the ***adjuvant*** compn. of the invention comprises a saponin and an immunostimulatory oligonucleotide, optionally with a carrier. Also provided by the disclosed invention are ***vaccines*** comprising the ***adjuvants*** of the present invention and an antigen. Further provided are methods of manuf. of the ***adjuvants*** and ***vaccines*** of the present invention and their use as medicaments. Methods of treating an individual susceptible to or suffering from a disease by the administration of the ***vaccines*** of the present invention are also provided.

L14 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2002:946065 Document No. 138:38056 Mutant forms of cholera holotoxin as an ***adjuvant*** . Green, Bruce A.; Holmes, Randall K.; Jobling, Michael G.; Zhu, Duzhang (American Cyanamid Company, USA; Government of the United States of America as Represented by the Uniformed Services University of the Health Sciences). PCT Int. Appl. WO 2002098369 A2 20021212, 88 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US21008 20020605. PRIORITY: US 2001-PV296531 20010607.

AB Mutant cholera holotoxins having single or double amino acid substitutions or insertions have reduced toxicity compared to the wild-type cholera holotoxin. The mutant cholera holotoxins are useful as ***adjuvants*** in antigenic compns. to enhance the immune response in a vertebrate host to a selected antigen from a pathogenic bacterium, virus, fungus, or

parasite; a cancer cell, a tumor cell, an allergen, or a self-mol.

L14 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:946064 Document No. 138:23652 Mutant forms of cholera holotoxin as an ***adjuvant*** . Green, Bruce A.; Holmes, Randall K.; Jobling, Michael G.; Zhu, Duzhang (American Cyanamid Company, USA; University of Colorado). PCT Int. Appl. WO 2002098368 A2 20021212, 89 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US20978 20020605. PRIORITY: US 2001-PV296537 20010607.
AB Mutant cholera holotoxins comprising a cholera toxin subunit A having single amino acid substitutions in the amino acid positions (16 or 72) or double amino acid positions (16 and 68) or (68 and 72) have reduced toxicity compared to the wild-type cholera holotoxin. The mutant cholera holotoxins are useful as ***adjuvants*** in immunogenic compns. to enhance the immune response in a vertebrate host to a selected antigen from a pathogenic bacterium, virus, fungus, or parasite, a cancer cell, a tumor cell, an allergen, or a self-mol.

L14 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:913846 Document No. 138:203298 Intranasal immunotherapy for the treatment of Alzheimer's disease: Escherichia coli LT and LT(R192G) as mucosal ***adjuvants*** . Lemere, Cynthia A.; Spooner, Edward T.; Leverone, Jodi F.; Mori, Chica; Clements, John. D. (Brigham and Women's Hospital, Center for Neurologic Diseases, Harvard Medical School, Boston, MA, 02115, USA). Neurobiology of Aging, 23(6), 991-1000 (English) 2002. CODEN: NEAGDO. ISSN: 0197-4580. Publisher: Elsevier Science Inc..
AB Alzheimer's disease (AD) is the most common form of dementia worldwide, yet there is currently no effective treatment or cure. Extracellular deposition of ***amyloid*** -.beta. protein (A.beta.) in brain is a key neuropathol. characteristic of AD. In 1999, Schenk et al. first reported that an injected A.beta. ***vaccine*** given to PDAPP mice, an AD mouse model displaying A.beta. deposition in brain, led to the lowering of A.beta. levels in brain. In 2000, we demonstrated that intranasal (i.n.) immunization with human synthetic A.beta.1-40 peptide for 7 mo led to a 50-60% redn. in cerebral A.beta. burden in PDAPP mice; serum A.beta. antibody titers were low (.apprx.26 .mu.g/mL). More recently, we have optimized our i.n. A.beta. immunization protocol in wild-type (WT) mice. When low doses Escherichia coli heat-labile enterotoxin (LT) were given as a mucosal ***adjuvant*** with A.beta. i.n., there was a dramatic 12-fold increase in A.beta. antibody titers in WT B6D2F1 mice treated two times per wk for 8 wk compared to those of mice receiving i.n. A.beta. without ***adjuvant*** . A non-toxic form of LT, designated LT(R192G), showed even better adjuvanticity; anti-A.beta. antibody titers were 16-fold higher than those seen in mice given i.n. A.beta. without ***adjuvant*** . In both cases, the serum A.beta. antibodies recognized epitopes within A.beta.1-15 and were of the Ig isotypes IgG2b, IgG1, IgG2a and low levels of IgA. This new and improved A.beta. ***vaccine*** protocol is now being tested in AD mouse models with the expectation that higher A.beta. antibody titers may be more effective in reducing cerebral A.beta. levels.

L14 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:880031 Document No. 137:336715 ***Vaccine*** for treatment of degenerative disease, autoimmune disease, or cancer. Connolly, Simon (UK). Brit. UK Pat. Appl. GB 2370770 A1 20020710, 37 pp. (English). CODEN: BAXXDU. APPLICATION: GB 2001-92 20010103.
AB The invention relates to a ***vaccine*** prepn. and methods for the treatment of degenerative diseases of humans, such as rheumatic diseases, autoimmune conditions, and malignant cell growths. The ***vaccine*** comprises live attenuated or dead Streptococcus, preferably .beta.-Hemolytic Group A Streptococcus, optionally together with bacteriophage which are assocd. therewith. The diseases discussed in this invention have been found to be fully or partly caused by infection with members of the Streptococcus family.

L14 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:822056 Document No. 138:54113 Age-related differences in the immune response to immunization with human A.beta.42 peptide. Pifer, Jeannette; Hennes, Jason L.; Lee, John M.; Witte, Pamela L. (Departments of Cell Biology, Neurobiology, & Anatomy, Loyola University Medical Center, Maywood, IL, USA). Journals of Gerontology, Series A: Biological Sciences and Medical Sciences, 57A(10), B355-B358 (English) 2002. CODEN: JGASFW. ISSN: 1079-5006. Publisher: Gerontological Society of America.
AB Several studies show that plaque burden is resolved in young to middle-aged ***amyloid*** precursor protein transgenic mice after rigorous immunization with A.beta.42 peptide. The authors detd. if wild-type 20-mo-old and 3-mo-old animals could produce high-titer antibody against A.beta.42 with a less strenuous immunization protocol. All treated young animals mounted a high-titer (20,000-50,000) response after 2 immunizations and sustained a strong response for 6 mo following the initial treatment with A.beta.42. However, 6 of 8 immunized aged animals did not respond after 3 immunizations. The 2 responding aged mice produced low-titer antibody (5000-10,000), which rapidly declined to control levels within 5 wk after the third immunization. Aged animals may require alternate strategies for successful vaccination, such as inclusion of stimulatory cytokines or better ***adjuvants*** .

L14 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:555371 Document No. 137:139348 Molecular antigen array for ***vaccines*** against infectious disease, cancer, allergies and autoimmune diseases. Maurer, Patrick; Lechner, Franziska; Ortmann, Rainer; Lueoend, Rainer; Staufenbiel, Matthias; Frey, Peter; Renner, Wolfgang A.; Bachmann, Martin; Tissot, Alain; Sebbel, Peter; Piossek, Christine (Cytos Biotechnology A.-G., Switz.; Novartis Pharma A.-G.). PCT Int. Appl. WO 2002056907 A2 20020725, 418 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-IB168 20020121. PRIORITY: US 2001-PV262379 20010119; US 2001-PV288549 20010504; US 2001-PV326998 20011005; US 2001-PV331045 20011107.
AB The present invention is related to the fields of mol. biol., virol., immunol. and medicine. The invention provides a compn. comprising an ordered and repetitive antigen or antigenic determinant array. The invention also provides a process for producing an antigen or antigenic determinant in an ordered and repetitive array. The ordered and repetitive antigen or antigenic determinant is useful in the prodn. of ***vaccines*** for the treatment of infectious diseases, the treatment of allergies and as a pharmaccine to prevent or cure cancer and to efficiently induce self-specific immune responses, in particular antibody responses.

L14 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:555369 Document No. 137:124189 ***Vaccine*** compositions comprising molecular antigen array against cancer, infection, and allergy. Renner, Wolfgang A.; Bachmann, Martin; Tissot, Alain; Maurer, Patrick; Lechner, Franziska; Sebbel, Peter; Piossek, Christine (Cytos Biotechnology A.-G., Switz.). PCT Int. Appl. WO 2002056905 A2 20020725, 442 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-IB166 20020121. PRIORITY: US 2001-PV262379 20010119; US 2001-PV288549 20010504; US 2001-PV326998 20011005; US 2001-PV331045 20011107.
AB The present invention is related to the fields of mol. biol., virol., immunol. and medicine. The invention provides a compn. comprising an

ordered and repetitive antigen or antigenic determinant array. The invention also provides a process for producing an antigen or antigenic determinant in an ordered and repetitive array. The ordered and repetitive antigen or antigenic determinant is useful in the prodn. of ***vaccines*** for the treatment of infectious diseases, the treatment of allergies and as a pharmaccine to prevent or cure cancer and to efficiently induce self-specific immune responses, in particular antibody responses.

L14 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:275751 Document No. 136:290805 Mucin binding proteins and their variants from Streptococcus pneumoniae and their use in diagnosis and treatment of infections. Green, Bruce A.; Masi, Amy W.; Reddy, Molakala S. (American Home Products Corporation, USA; The Research Foundation of S.U.N.Y.). PCT Int. Appl. WO 2002028351 A2 20020411, 71 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US31269 20011004. PRIORITY: US 2000-PV237888 20001004; US 2001-PV267104 20010207.
AB The present invention provides for amino acid and nucleic acid sequences of isolated mucin-binding proteins (MBP) from Streptococcus pneumoniae and fragments thereof. More specifically, mucin-binding proteins of 12 kDa and 14 kDa were identified using a 10-20% SDS-PAGE gel. Expression vectors, transfected host cells, methods for producing recombinant mucin-binding proteins, compns. comprising the proteins, and antibodies to the proteins also are contemplated. A method of inducing an immune response is described by the present invention. Screening and diagnosing methods are provided for otitis media, bacteremia pneumonia, meningitis, rhino sinusitis and lower respiratory tract infections using MBP of the present invention. In a specific embodiment, lysine variants of MBP are provided wherein the absence of at least one lysine residue decreases mucin-binding protein activity. Mucosal immunization with 12 kDa MBP was shown to reduce pneumococcal colonization in the mouse nasopharynx.

L14 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:142851 Document No. 136:215388 Immunogenic hepatitis B nucleocapsid protein (HBc) chimeric particles having enhanced stability. Birkett, Ashley J. (Apovia, Inc., USA). PCT Int. Appl. WO 2002014478 A2 20020221, 290 pp. DESIGNATED STATES: W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, MZ, NO, NZ, PL, RO, SG, SI, SK, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US41759 20010816. PRIORITY: US 2000-PV225843 20000816; US 2000-PV226867 20000822; US 2001-930915 20010815.
AB A chimeric, carboxy-terminal truncated hepatitis B virus nucleocapsid protein (core protein or HBc) is disclosed that is engineered for both enhanced stability of self-assembled particles and the display of an immunogenic epitope. The immunogenic epitope is a B cell epitope or T cell epitope derived from pathogen such as Streptococcus pneumonia, Cryptosporidium parvum, HIV, foot and mouth disease virus, influenza virus, Yersinia pestia, etc. The display of the immunogenic epitope is displayed in the immunogenic loop of HBc, whereas the enhanced stability of self-assembled particles is obtained by the presence of at least one heterologous cysteine residue near the carboxy-terminus of the chimer mol. Methods of making and using the chimers are also disclosed.

L14 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2002:107147 Document No. 136:166053 Innate immune system-directed ***vaccines*** . Medzhitov, Ruslan M. (Yale University, USA). PCT Int. Appl. WO 2002009748 A1 20020207, 139 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,

MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US24228 20010731. PRIORITY: US 2000-PV222042 20000731; US 2000-PV258329 20001228; US 2001-752832 20010103; US 2001-PV282604 20010409.

AB The present invention provides novel ***vaccines*** , method for the prodn. of such ***vaccines*** and methods of using such ***vaccines*** . The novel ***vaccines*** of the present invention combine both of the signals necessary to activate native T-cells - specific antigen and the co-stimulatory signal - leading to a robust and specific T-cell immune response. The ***vaccine*** comprises one or more PAMPs (pathogen-assocd. mol. pattern) conjugated to one or more antigen; PAMP/antigen fusion protein; or a modified antigen comprising a leader sequence fused to a lipidation or glycation consensus sequence and the antigen.

L14 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2001:935433 Document No. 136:68694 QS-21 and IL-12 as an ***adjuvant*** combination. Hancock, Gerald E. (American Cyanamid Company, USA). PCT Int. Appl. WO 2001097841 A2 20011227, 53 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US19805 20010621. PRIORITY: US 2000-PV213143 20000622.

AB The author discloses the ***adjuvant*** application of a combination of interleukin-12 and QS-21. In one example, the humoral immune response to the F protein of respiratory syncytial virus was shown to be enhanced by a suboptimal concn. of QS-21 in combination with increasing amts. of interleukin-12.

L14 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2001:868521 Document No. 136:36318 Synthetic immunogenic but non-amyloidogenic peptides homologous to ***amyloid*** .beta. for induction of an immune response to ***amyloid*** .beta. and ***amyloid*** deposits. Frangione, Blas; Wisniewski, Thomas; Sigurdsson, Einar M. (New York University, USA). PCT Int. Appl. WO 2001090182 A2 20011129, 69 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US16322 20010522. PRIORITY: US 2000-PV205578 20000522.

AB The present invention relates to synthetic immunogenic but non-amyloidogenic peptides homologous to ***amyloid*** .beta. which can be used alone or conjugated to an immunostimulatory mol. in an immunizing compn. for inducing an immune response to ***amyloid*** .beta. peptides and ***amyloid*** deposits. These peptides may be used in ***vaccines*** for Alzheimer's disease.

L14 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2001:833125 Document No. 136:4705 Molecular antigen array. Sebbel, Peter; Dunant, Nicolas; Bachmann, Martin; Tissot, Alain; Lechener, Franziska (Cytos Biotechnology A.-G., Switz.). PCT Int. Appl. WO 2001085208 A2 20011115, 287 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML,

MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-IB741 20010502. PRIORITY: US 2000-PV202341 20000505.

AB The invention provides compns. and processes for the prodn. of ordered and repetitive antigen or antigenic determinant arrays. The compns. of the invention are useful for the prodn. of ***vaccines*** for the prevention of infectious diseases, the treatment of allergies and the treatment of cancers. Various embodiments of the invention provide for a core particle that is coated with any desired antigen in a highly ordered and repetitive fashion as the result of specific interactions.

L14 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2001:545831 Document No. 135:121188 ***Vaccines*** against neurodegenerative disorders. Srivastava, Pramod K. (University of Connecticut Health Center, USA). PCT Int. Appl. WO 2001053457 A2 20010726, 47 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US1665 20010118. PRIORITY: US 2000-489219 20000121.

AB The present invention relates to pharmaceutical compns. comprising antigenic mols. for use as ***vaccines*** for the treatment and prevention of neurodegenerative disorders and diseases, such as Alzheimer's Disease. The invention further relates to methods for the use of such pharmaceutical compns. as immunotherapeutic agents for treating and protecting against such neurodegenerative disorders and disease.

L14 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2000:861516 Document No. 134:28431 Prevention and treatment of amyloidogenic disease. Schenk, Dale B. (Neuralab Limited, Bermuda). PCT Int. Appl. WO 2000072876 A2 20001207, 140 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US15239 20000601. PRIORITY: US 1999-PV137010 19990601.

AB The authors discloses methods for immunotherapy of ***amyloid*** diseases, including Alzheimer's disease, prion diseases, and familial ***amyloid*** neuropathies. In one example, Alzheimer's disease-prone mice were immunized with ***amyloid*** peptide (A.beta.1-42). In contrast to control mice, treated mice exhibited a lack of ***amyloid*** plaques, neuritic pathol., and astrocytosis. In a second example, Alzheimer's disease-prone mice were passively immunized with antibodies to ***amyloid*** peptides. Treated mice exhibited a significant decrease in cerebral A.beta. levels and a redn. in ***amyloid*** load.

L14 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN

2000:824121 Document No. 134:16517 3-O-deacylated monophosphoryl lipid A ***adjuvants*** . Hagen, Michael (American Cyanamid Company, USA). PCT Int. Appl. WO 2000069456 A2 20001123, 129 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US13156 20000512. PRIORITY: US 1999-PV133963 19990513.

AB The author discloses the use of 3-O-deacylated monophosphoryl lipid A or monophosphoryl lipid A and derivs. and analogs, in combination with a cytokine or lymphokine (e.g., GM-CSF or interleukin-12) as ***adjuvants*** for enhancing the humoral and cellular immune responses in a vertebrate host to a selected antigen. In one example, mice were immunized with an envelope peptide of HIV in an emulsion contg. 3-O-deacylated monophosphoryl lipid A and GM-CSF. Both the IgG and spleen responses were enhanced relative to controls without ***adjuvants*** and CFA/IFA.

L14 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2000:756545 Document No. 133:340220 ***Adjuvant*** comprising a saponin and an immunostimulatory oligonucleotide for manufacture of ***vaccines*** . Friede, Martin; Garcon, Nathalie; Hermand, Philippe (Smithkline Beecham Biologicals S. A., Belg.). PCT Int. Appl. WO 2000062800 A2 20001026, 52 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP2920 20000404. PRIORITY: GB 1999-8885 19990419; US 1999-301829 19990429.

AB The present invention relates to ***adjuvant*** compns. which are suitable to be used in ***vaccines*** . In particular, the ***adjuvant*** compns. of the present invention comprises a saponin and an immunostimulatory oligonucleotide, optionally with a carrier. Also provided by the present invention are ***vaccines*** comprising the ***adjuvants*** of the present invention and an antigen. Further provided are methods of manuf. of the ***adjuvants*** and ***vaccines*** of the present invention and their use as medicaments. Methods of treating an individual susceptible to or suffering from a disease by the administration of the ***vaccines*** of the present invention are also provided.

L14 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2000:608610 Document No. 133:206755 Immunogens comprising a peptide and a carrier derived from Haemophilus influenzae protein D. Coste, Michel; Lobet, Yves; Van-Mechelen, Marcelle Paulette; Verriest, Christophe (Smithkline Beecham Biologicals S.A., Belg.). PCT Int. Appl. WO 2000050077 A1 20000831, 53 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-EP1457 20000222. PRIORITY: GB 1999-4405 19990225; GB 1999-4408 19990225; GB 1999-4412 19990225; GB 1999-19260 19990813.

AB The present invention provides peptide immunogens linked to a carrier wherein the carrier is derived from Haemophilus Influenzae Protein D or fragments thereof. Compns comprising the antigen peptide, protein D epitope or mimotope, and immune ***adjuvant*** (e.g. saponin, aluminum salt, oil in water emulsion, or liposome) are useful for treating infection or chronic diseases.

L14 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
2000:314719 Document No. 132:346621 Biological materials and methods useful in the diagnosis and treatment of diseases. Collinge, John; Clarke, Anthony Russell; Jackson, Graham Stuart (Imperial College Innovations Limited, UK). PCT Int. Appl. WO 2000026238 A2 20000511, 115 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-GB3617 19991102. PRIORITY: GB 1998-24091 19981104; GB 1999-6217 19990318.

AB The present invention relates to a method of making a .beta.-form of a prion protein which preferably has more .beta.-sheet than .alpha.-helix structure and is sol. in the absence of a denaturant and/or is non-aggregated and exhibits partial resistance to digestion with proteinase K. The invention also relates to use of the .beta.-form in medicine, esp. for raising antibodies useful in the treatment and/or diagnosis of prion diseases. The invention also relates to methods of screening for compds. which are capable of inhibiting and/or reversing the

conversion of the native .alpha.-form of a prion protein to a .beta.-form, and to uses of identified compds. in medicine.

L14 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
1999:375416 Document No. 131:27965 Prevention and treatment of amyloidogenic disease, especially Alzheimer's disease, based on induction of anti-***amyloid*** immune response. Schenk, Dale B. (Athena Neurosciences, Inc., USA). PCT Int. Appl. WO 9927944 A1 19990610, 113 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US25386 19981130. PRIORITY: US 1997-67740 19971202; US 1998-80970 19980407.
AB The invention provides compns. and methods for treatment of amyloidogenic diseases. The methods entail administering an agent that induces a beneficial immune response against an ***amyloid*** deposit in the patient. The methods are particularly useful for prophylactic and therapeutic treatment of Alzheimer's disease. In such methods, a suitable agent is A.beta. peptide or an antibody thereto.

L14 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
1997:389189 Document No. 127:4085 Composition and methods for enhancing immune responses mediated by antigen-presenting cells. Sanderson, Sam D.; Hollingsworth, Michael A.; Tempero, Richard A. (University of Nebraska Board of Regents, USA; Sanderson, Sam D.; Hollingsworth, Michael A.; Tempero, Richard A.). PCT Int. Appl. WO 9714426 A1 19970424, 60 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US16825 19961018. PRIORITY: US 1995-5727 19951020.
AB Mol. ***adjuvants*** are disclosed comprising an antigen presenting cell-targeting ligand functionally linked to an immunogen, e.g. tumor assocd. antigens, bacterial or viral antigens, etc. The mol. ***adjuvant*** comprises a targeting ligand to immunomodulatory receptor of antigen-presenting cell selected from C5a receptor, interferon .gamma. receptor, CD21 receptor, CD64 receptor, and CD23 receptor. Methods are disclosed for delivery of these mol. ***adjuvants*** to patients resulting in the transduction of activating signals to the targeted antigen presenting cell, thereby enhancing the immune response to the co-delivered immunogen, e.g. human mucin-1, serum ***amyloid*** A, tumor-specific antigen, or other.

L14 ANSWER 26 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
1986:417737 Document No. 105:17737 Studies on type II collagen-induced arthritis in mice. Paska, W.; McDonald, K. J.; Croet, M. (Immunobiol. Dep., Glaxo Group Res. Ltd., Greenford/Middlesex, UB6 0HE, UK). Agents and Actions, 18(3-4), 413-20 (English) 1986. CODEN: AGACBH. ISSN: 0065-4299.
AB A consistent and reproducible polyarthritis was induced in mice by immunizing them with type-II collagen in Complete Freunds ***adjuvant*** (CFA) and Bacillus Calmette-Guerin (BCG) ***vaccine*** . Several inbred strains of mice were investigated for the ability to develop collagen-induced arthritis (CIA); DBA/I mice (II-2q) produced the highest incidence and the most severe arthritis of all the strains examd. Viable BCG ***vaccine*** was essential for the induction of a reproducible disease in this strain. The effects of some anti-inflammatory and antirheumatic compds. were examd. on the developing and established lesions of CIA. These effects were detd. by assessing paw inflammation using a subjective scoring system and measuring foot wt. Furthermore, levels of serum ***amyloid*** P component (SAP) were also detd. Benoxaprofen [51234-28-7], cyclophosphamide [50-18-0], indomethacin [53-86-1], and prednisolone [50-24-8] inhibited paw inflammation in the developing disease, whereas the antirheumatic compds. auranofin [34031-32-8] and D-penicillamine [52-67-5] exacerbated the paw inflammation. Cyclophosphamide and prednisolone inhibited established lesions but only prednisolone prevented the development of further lesions in established disease. The SAP levels in the prednisolone-treated group were also reduced. Auranofin treatment exacerbated the inflammation of

both established and developing lesions in the same animal. D-Penicillamine was inactive in the established disease.

L14 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
1978:454053 Document No. 89:54053 Effect of papain on experimental amyloidosis. Kopolovicz, J.; Fields, M.; Laufer, A. (Dep. Pathol., Hadassah Univ. Hosp., Jerusalem, Israel). Experientia, 34(4), 524-6 (English) 1978. CODEN: EXPEAM. ISSN: 0014-4754.
AB Exptl. amyloidosis was induced in mice by repeated injections of complete Freud's ***adjuvant*** (CFA) reinforced with a bacterial ***vaccine*** . Papain [9001-73-4] was administered i.p. at various time intervals during the treatment with CFA. Amyloidosis was found only in the spleen and the liver. No statistically significant differences were found between the papain-treated and the control groups. It is assumed that, although papain released the polysaccharide moiety from the polysaccharide-protein complex, the released polysaccharides were most probably bound by electrostatic forces to the ***amyloid*** fibers and did not interfere with amyloidogenesis.

L14 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
1977:11912 Document No. 86:11912 The effect of beta aminoproprionitrile (BAPN) on experimental amyloidosis. Schechter, D.; Fields, M.; Laufer, A. (Dep. Pathol., Rothschild-Hadassah Univ. Hosp., Jerusalem, Israel). British Journal of Experimental Pathology, 56(5), 466-70 (English) 1975. CODEN: BJEPA5. ISSN: 0007-1021.
AB Exptl. amyloidosis was induced in mice with repeated injections of complete Freund's ***adjuvant*** (CFA) reinforced with bacterial ***vaccine*** . .beta.-Aminoproprionitrile fumarate (BAPN) [2079-89-2] (1.0 mg/g) administered in a mixt. with CFA or on its own before the injection of CFA reduced the incidence of amyloidosis. The redn. in the incidence of amyloidosis following the administration of BAPN may be due to its inhibitory effect on the oxidative deamination of amino acids, which presumably inhibit crosslinking of ***amyloid*** fibrils or interfere with metabolic pathways which involve the formations of mucopolysaccharide formation. It is suggested that the defective formation of the mucopolysaccharide- ***amyloid*** protein complex inhibits ***amyloid*** deposition and induces the activity of .beta.-glucuronidase [9001-45-0] obsd. in the present study. The reduced incidence of amyloidosis following BAPN administration cannot be due to lysosomal enzyme degrdn. of the ***amyloid*** as the activity of cathepsin D [9025-26-7] and acid phosphatase [9001-77-8] is decreased during this process.

L14 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2003 ACS on STN
1963:61757 Document No. 58:61757 Original Reference No. 58:10593h,10594a The cytologic reaction of the spleen in experimental amyloidosis in mice. Zlotnick, Avinoam; Tal, Chloe Blood, 16, 1491-8 From: Biol. Abstr. 36, Abstr. No. 6984(1961). (Unavailable) 1960. CODEN: BLOOAW. ISSN: 0006-4971.
AB Of 61 mice injected with ***adjuvant*** , TAB ***vaccine*** , and Merthiolate, ***amyloid*** developed in the spleen in 48. Varying degrees of plasma cell hyperplasia were noted in 46, and increased granulopoiesis in 37. Flame-cell transformation of some of the plasma cells was noted in 28. In the injected animals the serums showed an increase in albumin and globulin. Animals receiving ***adjuvant*** alone showed an increase in .beta.-globulins, while animals receiving TAB plus ***adjuvant*** or TAB alone showed increase .gamma.-globulins.

L14 ANSWER 30 OF 35 MEDLINE on STN
2003019442 Document Number: 22359436. PubMed ID: 12470794. Intranasal immunotherapy for the treatment of Alzheimer's disease: Escherichia coli LT and LT(R192G) as mucosal ***adjuvants*** . Lemere Cynthia A; Spooner Edward T; Leverone Jodi F; Mori Chica; Clements John D. (Center for Neurologic Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, MA 02115, USA.. lemere@cnd.bwh.harvard.edu) . NEUROBIOLOGY OF AGING, (2002 Nov-Dec) 23 (6) 991-1000. Journal code: 8100437. ISSN: 0197-4580. Pub. country: United States. Language: English.
AB Alzheimer's disease (AD) is the most common form of dementia worldwide, yet there is currently no effective treatment or cure. Extracellular deposition of ***amyloid*** -beta protein (Abeta) in brain is a key neuropathological characteristic of AD. In 1999, Schenk et al. first

reported that an injected Abeta ***vaccine*** given to PDAPP mice, an AD mouse model displaying Abeta deposition in brain, led to the lowering of Abeta levels in brain. In 2000, we demonstrated that intranasal (i.n.) immunization with human synthetic Abeta1-40 peptide for 7 months led to a 50-60% reduction in cerebral Abeta burden in PDAPP mice; serum Abeta antibody titers were low (approximately 26 microg/ml). More recently, we have optimized our i.n. Abeta immunization protocol in wild-type (WT) mice. When low doses Escherichia coli heat-labile enterotoxin (LT) were given as a mucosal ***adjuvant*** with Abeta i.n., there was a dramatic 12-fold increase in Abeta antibody titers in WT B6D2F1 mice treated two times per week for 8 weeks compared to those of mice receiving i.n. Abeta without ***adjuvant*** . A non-toxic form of LT, designated LT(R192G), showed even better adjuvanticity; anti-Abeta antibody titers were 16-fold higher than those seen in mice given i.n. Abeta without ***adjuvant*** . In both cases, the serum Abeta antibodies recognized epitopes within Abeta1-15 and were of the immunoglobulin (Ig) isotypes IgG2b, IgG1, IgG2a and low levels of IgA. This new and improved Abeta ***vaccine*** protocol is now being tested in AD mouse models with the expectation that higher Abeta antibody titers may be more effective in reducing cerebral Abeta levels.

L14 ANSWER 31 OF 35 MEDLINE on STN
2002219732 Document Number: 21953391. PubMed ID: 11956972. Alzheimer's ***vaccine*** : a cure as dangerous as the disease?. Munch G; Robinson S R. (Neuroimmunological Cell Biology Unit, Interdisciplinary Center for Clinical Research (IZKF), University of Leipzig, Federal Republic of Germany.. mueg@medizin.uni-leipzig.de) . JOURNAL OF NEURAL TRANSMISSION, (2002 Apr) 109 (4) 537-9. Ref: 6. Journal code: 9702341. ISSN: 0300-9564. Pub. country: Austria. Language: English.
AB Studies in transgenic mouse models of Alzheimer's disease suggested the potential for a ***vaccine*** development. However, some patients in the human clinical trials developed symptoms of brain inflammation, demonstrating the high risk of a deliberately induced auto-immune response.

L14 ANSWER 32 OF 35 MEDLINE on STN
2002139418 Document Number: 21864611. PubMed ID: 11875473. Set back to Alzheimer ***vaccine*** studies. Birmingham Karen; Frantz Simon. NATURE MEDICINE, (2002 Mar) 8 (3) 199-200. Journal code: 9502015. ISSN: 1078-8956. Pub. country: United States. Language: English.

L14 ANSWER 33 OF 35 MEDLINE on STN
86319647 Document Number: 86319647. PubMed ID: 3092598. Studies on type II collagen induced arthritis in mice. Paska W; McDonald K J; Croft M. AGENTS AND ACTIONS, (1986 Jun) 18 (3-4) 413-20. Journal code: 0213341. ISSN: 0065-4299. Pub. country: Switzerland. Language: English.
AB A consistent and reproducible polyarthritis was induced in mice by immunizing them with type II collagen in Complete Freunds ***adjuvant*** (CFA) and Bacillus Calmette-Guerin (BCG) ***vaccine*** . Several inbred strains of mice were investigated for the ability to develop collagen induced arthritis (CIA). DBA/1 mice (H-2q) produced the highest incidence and the most severe arthritis of all the strains examined. Viable BCG ***vaccine*** was essential for the induction of a reproducible disease in this strain. The effects of some anti-inflammatory and anti-rheumatic compounds were examined on the developing and established lesions of CIA. These effects were determined by assessing the paw inflammation using a subjective scoring system and measuring foot weight. Furthermore, levels of serum ***amyloid*** P component (SAP) were also determined. Benoxaprofen, cyclophosphamide, indomethacin and prednisolone inhibited the paw inflammation in the developing disease whilst the anti-rheumatic compounds auranofin and D-penicillamine exacerbate the paw inflammation. Cyclophosphamide and prednisolone inhibited the established lesions but only prednisolone prevented the development of further lesions in the established disease. The SAP levels in the prednisolone treated group were also reduced. Auranofin treatment exacerbated the inflammation of both the established and the developing lesions in the same animal. D-penicillamine was inactive in the established disease.

L14 ANSWER 34 OF 35 MEDLINE on STN
78148255 Document Number: 78148255. PubMed ID: 639956. Effect of papain

on experimental amyloidosis. Kopolovicz J; Fields M; Laufer A. EXPERIENTIA, (1978 Apr 15) 34 (4) 524-6. Journal code: 0376547. ISSN: 0014-4754. Pub. country: Switzerland. Language: English.

AB Experimental amyloidosis was induced in mice by repeated injections of complete Freund's ***adjuvant*** (CFA) reinforced with a bacterial ***vaccine*** . Papain was administered i.p. at various time intervals during the treatment with CFA. Amyloidosis was found only in the spleen and the liver. No statistically significant differences were found between the papain-treated and the control groups. It is assumed that, although papain releaseed the polysaccharide moiety from the polysaccharide protein complex, the released polysaccharides were most probably bound by electrostatic forces to the ***amyloid*** fibres, and did not interfere with amyloidogenesis.

L14 ANSWER 35 OF 35 MEDLINE on STN

76114715 Document Number: 76114715. PubMed ID: 1212427. The effect of beta aminoproprionitrile (BAPN) on experimental amyloidosis. Schechter D; Fields M; Laufer A. BRITISH JOURNAL OF EXPERIMENTAL PATHOLOGY, (1975 Oct) 56 (5) 466-70. Journal code: 0372543. ISSN: 0007-1021. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Experimental amyloidosis was induced in mice with repeated injections of complete Freund's ***adjuvant*** (CFA) reinforced with bacterial ***vaccine*** . BAPN administered in a mixture with CFA or on its own before the injection of CFA reduced the incidence of amyloidosis. The reduction in the incidence of amyloidosis following the administration of BAPN may be due to its inhibitory effect on the oxidative deamination of amino acids, which presumably inhibit cross-linking of ***amyloid*** fibrils or interfere with metabolic pathways which involve the formations of mucopolysaccharide formation. It is suggested that the defective formation of the mucopolysaccharide- ***amyloid*** protein complex inhibits ***amyloid*** deposition and induces the activity of beta glucuronidase observed in the present study. The reduced incidence of amyloidosis following BAPN adminsitration cannot be due to lysosomal enzyme degradation of the ***amyloid*** as the activity of cathepsin D and acid phosphatase is decreased during this process.